## REMARKS

Reconsideration of the present application in view of the above amendments and following remarks is requested respectfully.

Claims 25 and 27 to 32 are pending. Claim 25 has been amended. No claims have been added, and Claims 26 and 33 have been canceled.

### Summary of the Invention

The present invention is generally directed to kappa agonist compounds and their use in the treatment of certain disease states. In particular, the only remaining pending independent claim (Claim 25) importantly and critically defines a ***method of treating or preventing pruritus in a mammal in need of such prevention or treatment***. Independent Claim 25, as amended herein, further importantly and critically recites that the method comprises administering to the mammal a ***non-peptide kappa opiate receptor agonist***. As discussed in detail below, the cited prior art neither discloses nor suggests these, as well as other important and critical features as employed by applicants in the context of the present invention.

### Discussion of the Art Rejections

The Office Action includes rejections under Sections 102 and 103 which are discussed in detail below.

**Rejection Under Section 102**

Claim 33 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Horwell et al., U.S. Patent No. 4,663,343 ("Horwell"). It is basically asserted in the Office Action that Horwell teaches applicants' defined compositions.

Applicants respectfully disagree with this rejection, and submit that Claim 33 defines over Horwell. Nevertheless, in an effort to facilitate prosecution of the present application, Claim 33 has been canceled. In view of this cancellation, reconsideration and withdrawal of the rejection under Section 102 are requested respectfully.

**Rejection Under Section 103**

Claims 25 to 32 have been rejected under 35 U.S.C. § 103 as being unpatentable over Dooley et al., U.S. Patent No. 5,610,271 ("Dooley"). It is basically asserted in the Office Action that applicants' invention would have been *prima facie* obvious based on the teachings of this patent. Applicants respectfully traverse the rejection.

Dooley is directed to opioid peptides which are disclosed as being capable of inhibiting the binding of the κ-selective opioid ligand [$^3$H]-U69,593 (column 2, lines 10 to 12). Dooley teaches that the disclosed opioid peptides may be useful in *in vitro* assays to study subtypes of the κ receptor, and in *in vivo* applications, for example, to localize opioid receptor subtypes, as analgesics, and to treat pathologies associated with other compounds that interact with the opioid receptor system (column 4, line 66 to column 5, line 29).

As recognized by the Examiner at page 6 of the Office Action, Dooley fails to disclose or suggest, *inter alia*, methods of treating pruritus by administering a kappa opiate receptor agonist as described and claimed in the present application. Applicants submit respectfully that in the absence of a disclosure in Dooley or a convincing line of reasoning which suggests the modification, the obviousness standard upon which the present rejection is based is the "obvious to try" standard. It is well-settled that this is *not* an appropriate standard -- the art must suggest with some degree of *certainty* the success of that which applicants are claiming as their invention. *In re Dow Chem.*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988); and *In re Tomlinson*, 150 U.S.P.Q. 623 (C.C.P.A. 1966).

To further distinguish over Dooley, independent Claim 25 has been amended to define non-peptide kappa opiate receptor agonists.[1] As noted above, Dooley is directed to the use of opioid peptides. Applicants submit respectfully that there is no disclosure or suggestion whatsoever in Dooley regarding the prevention or treatment of pruritus using non-peptide kappa opiate receptor agonists, as defined in independent Claim 25, as amended herein.

In view of the foregoing discussion, reconsideration and withdrawal of the Section 103 rejection are requested respectfully.

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[1] This amendment is supported in the application, for example, at page 12, lines 2 to 3.

**Discussion of the Rejections for Obviousness-type Double Patenting**

Without commenting on the appropriateness of the obviousness-type double patenting rejections in view of claims of issued patents commonly owned by the assignee of the present application, applicants propose to file a Terminal Disclaimer under 37 CFR 1.321(c) upon the withdrawal of the remaining rejections.

**Discussion of the Rejections Under Section 112**

With regard to the rejection of Claims 25 to 33 under 35 U.S.C. § 112, first paragraph, applicants acknowledge and appreciate the Examiner's favorable ruling that the specification is enabling for particular compounds as set forth at pages 99 to 112 of the application. Applicants disagree respectfully, however, with the statement that enablement is provided for such compounds only. It is submitted respectfully that the present application contains extensive teachings which would enable a skilled artisan to make and use the full scope of the compounds defined in the pending claims. In this regard, the Examiner's attention is directed respectfully to the teachings in the present application, for example, at page 8, line 1 to page 134, line 14. Applicants provide therein an extensive discussion of compounds which are encompassed by the presently claimed kappa opiate agonists. Exemplary methods for making the involved compounds are disclosed in the present application, for example, at page 12, line 13 to page 16; page 20, line 3 to page 23; page 25, lines 1 to 5; and page 27. The working examples at pages 30 to 92 describe the preparation of numerous exemplary kappa opiate agonist compounds.

With respect to methods of use, applicants provide a detailed background discussion of the biochemical and physiological aspects of kappa receptors and their implication in disorders involving itch (page 1, line 17 to page 7, line 10). Extensive teachings are provided in the present application respecting the prevention or treatment of itch employing compounds as described in the present application. In this connection, the Examiner's attention is directed respectfully to the test procedures at page 112, line 3 to page 113, line 14 of the application which may be used to evaluate the pharmacological activity and selectivity of compounds of the present invention.

Formulations with kappa opiate receptors as described and claimed in the present application, including systemic, local and topical formulations, are set forth at page 113, line 15 to page 121, line 4. Applicants further provide information regarding formulations in the form of lotions (page 121, line 5 to page 124, line 3), creams (page 121, lines 5 to 14), solutions and suspensions (page 124, line 15 to page 126, line 4), gels (page 126, lines 5 to 14), and solids (page 126, lines 15 to 30). Information regarding optional additional ingredients, combinations and kits, articles of manufacture, methods of treatment, and exemplary formulations are set forth at page 126, line 31 to page 134, line 14.

Although couched in terms of Section 112, applicants submit respectfully that the Examiner's rejection is actually based on the utility aspects of 35 U.S.C. § 101. In this regard, the Examiner's attention is directed respectfully to MPEP § 706.03(a)(1), as well as the Utility Examination Guidelines, at 6-7 Legal Analysis (1995), which provide that if the

asserted utility of a compound is credible on its face to persons skilled in the art, then a rejection for lack of utility is inappropriate. Indeed, a utility is considered to be incredible if:

(a) the logic underlying the assertion is seriously flawed; or

(b) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion.

*See* Examination Utility Guidelines, at 8, Legal Analysis (1995). Applicants submit respectfully that the present application contains extensive teachings such that one of ordinary skill in the art would conclude that the logic underlying applicant's asserted utility is not seriously flawed, and that the facts upon which the assertion is based, and the underlying logic, are not inconsistent.

It is well-settled that the first paragraph of Section 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance. *In re Marzocchi and Horton*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). The Patent Office has the burden of giving reasons, supported by the record as whole, why the specification is not enabling. *In re Armbruster*, 185 U.S.P.Q. 152 (C.C.P.A. 1975). It is submitted respectfully that this burden has not been met in the present case. Moreover, the fact that some experimentation may be involved in identifying compounds which may be used to treat or prevent itch does not, *a priori*, mean that the type and amount of experimentation is undue. *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1986).

Applicants respectfully traverse the rejection based on the term "substantially". It is submitted respectfully that the present application contains extensive teachings regarding opiates and central nervous system side effects associated therewith. See, e.g., page 1 to 7 in the present application. Applicants submit respectfully that one of ordinary skill in the art to which the present invention is directed, including the field of organic compounds for the treatment of itch, would have no difficulty in ascertaining the scope and content of the present claims.

In view of the objection based on improper claim dependency, Claim 26 has been canceled.

In view of the above amendments and remarks, reconsideration and withdrawal of the rejections under Section 112 are requested respectfully.

**Miscellaneous**

The remaining amendments to independent Claim 25 are to correct minor typographical errors.

**Conclusion**

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable reconsideration of the

rejections and an allowance of all of pending Claims 25 and 27 to 32 are requested respectfully.

Respectfully submitted,

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**Version with Markings to Show Changes Made**

**In the Claims**

25. (Amended) A method of treating or preventing [pruritis] pruritus in a mammal in need of such prevention or treatment, said method comprising administering to said mammal a non-peptide kappa opiate receptor agonist, or a pharmaceutically acceptable salt thereof, that is substantially devoid of central nervous system effects, in a pharmaceutically acceptable carrier.

Cancel Claims 26 and 33, without prejudice.